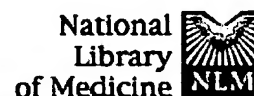


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Lck inhibitors as a therapeutic approach to autoimmune disease and transplant rejection.

Kamens JS, Ratnofsky SE, Hirst GC.

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T-cells play an important role in the pathogenesis of many diseases. These include diseases with large commercial markets and also with significant unmet medical needs, such as rheumatoid arthritis and asthma in addition to those with smaller markets such as organ transplantation, multiple sclerosis, inflammatory bowel diseases, type 1 diabetes, systemic lupus erythematosus and psoriasis. The use of currently available immunomodulatory agents is often limited by the appearance of dose-limiting side effects that result from the actions of these agents on non-lymphoid tissues. LSTRA cell kinase (lck), one of eight known members of the human src family of non-transmembrane protein tyrosine kinases, has a pivotal role in T-cell signaling. Lck expression is restricted to lymphoid cells, so an lck-selective inhibitor would be expected to have a significantly improved safety profile for the treatment of T-cell-driven diseases.

PMID: 11717807 [PubMed - indexed for MEDLINE]

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Src kinase-mediated signaling in leukocytes.

Korade-Mirnic Z, Corey SJ.

Department of Pediatrics and Pharmacology, University of Pittsburgh School of Medicine, Pennsylvania, USA.

A concert of antigens, antibodies, cytokines, adhesion molecules, lipid factors, and their different receptors mediate leukocyte development and inflammatory responses. Regardless of the stimulus and receptor type, members of the Src family of protein tyrosine kinases (PTKs) play a critical role in initiating the numerous intracellular signaling pathways. Recruited and activated by the receptor, these Src PTKs amplify and diversify the signal. Multiple pathways arise, which affect cell migration, adhesion, phagocytosis, cell cycle, and cell survival. Essential nonredundant properties of Src PTKs have been identified through the use of gene targeting in mice or in the somatic cell line DT40. Because of their role in mediating leukocyte proliferation and activation, Src PTKs serve as excellent drug targets. Inhibitors of Src family members and dependent pathways may be useful in the treatment of human diseases similar to drugs known to inhibit other signal transduction pathways.

Publication Types:

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